



NOTES DYSLIPIDEMIA

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- **Metabolic disorders:** abnormal lipid levels, with ↑ cardiovascular, other disease risk
- **Lipids:** water-insoluble organic molecules contribute to normal metabolic process
 - Building blocks for cell membranes
 - Energy source
 - Fat-soluble vitamin absorption (needed)
 - Key molecule components (e.g. steroids, prostaglandins, bile acid)
 - Fat storage
- **Lipoproteins:** triacylglycerol (TAG), cholesterol, phospholipids, apolipoproteins
- Classified according physicochemical characteristics
 - Lipid density, the apolipoproteins types contained (↓ density → ↑ lipid relative to protein)
- **Lipoprotein types:** chylomicrons, very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL)
- Optimal lipid levels
 - **Total cholesterol:** 75–169mg/dL (ages ≤ 20 years); 100–199mg/dL (ages > 21 years)
 - **LDL:** < 70mg/dL (cardiovascular disease/very high risk individuals), < 100mg/dL (individuals with multiple cardiovascular disease risk-factors), < 130mg/dL (low cardiovascular disease risk individuals)
 - **HDL:** > 40mg/dL
 - **Triglycerides:** < 150mg/dL

TYPES

- Types organized by Fredrickson classification

Type I

- ↑ triglycerides > 99th percentile; ↑

chylomicron level

Type IIa

- Total cholesterol level > 90th percentile; ↑ LDL level; familial hypercholesterolemia

Type IIb

- Total cholesterol/triglyceride level > 90th percentile; ↑ LDL, VLDL levels; combined hyperlipoproteinemia

Type III

- Total cholesterol, triglyceride levels > 90th percentile; ↑ VLDL remnants, chylomicron levels; familial dysbetalipoproteinemia

Type IV

- Total cholesterol level > 90th percentile, triglyceride level > 90th percentile likely; ↑ VLDL, low HDL level; endogenous hyperlipidemia

Type V

- Triglyceride level > 99th percentile; ↑ VLDL, chylomicron levels; familial hypertriglyceridemia

RISK FACTORS

- Western diet (e.g. ↑ refined carbohydrate, ↑ calorie, ↑ dietary fat levels)
- Physical inactivity
- Risk ↑ with age
- Genetic/epigenetic influence

COMPLICATIONS

- Atherosclerosis → cardiovascular, cerebrovascular disease; pancreatitis, cholelithiasis (some cases)

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SIGNS & SYMPTOMS

- Asymptomatic until atherosclerosis progresses, produces complications
- Abdominal adiposity
 - Dyslipidemia correlation
- Lipid-related skin eruptions (e.g. xanthomas)
- Corneal arcus
 - Lipid deposition in peripheral cornea
- Clinical presentation suggests lipid-related vascular disease

DIAGNOSIS

LAB RESULTS

- Genetic testing as indicated

Blood studies

- Lipid profile

OTHER DIAGNOSTICS

- Pooled risk calculation: lipid levels + variables (age, sex, blood pressure, blood glucose level, smoking status)

TREATMENT

MEDICATIONS

- Hyperlipidemia
- Low, moderate, high statin therapy based on risk
- Non-statin therapy (bile acid sequestrants, fibrates)

OTHER INTERVENTIONS

- Risk reduction (hyperlipidemia)

ABETALIPOPROTEINEMIA

osms.it/abetalipoproteinemia

PATHOLOGY & CAUSES

- Rare **autosomal-recessive** disorder
 - MTP gene mutation in encoding microsomal triglyceride transfer protein (MTP)
 - AKA Bassen–Kornzweig disease
- MTP: required for hepatic, intestinal assembly of **apolipoprotein B** (apo B), lipids → ↓ **serum apo B-containing lipoproteins** (e.g. chylomicrons, LDL, VLDL) → impaired fat-soluble vitamin (A, D, E, K) transport
 - **Vitamin E** most susceptible to **deficiency**
 - Normally transported from small intestine to liver by chylomicrons, delivered to peripheral tissues via VLDLs

COMPLICATIONS

- Malabsorption, failure to thrive; retinal degeneration, ophthalmoplegia; peripheral neuropathy; cerebellar dysfunction (Friedreich-type spinocerebellar ataxia)

SIGNS & SYMPTOMS

- **Impaired fat absorption**
 - Initially presents (**infancy**) with gastrointestinal symptoms
 - e.g. poor feeding/weight gain, **failure to thrive**, gastrointestinal problems (e.g. nausea, abdominal distension, **steatorrhea**)
- Neurological (related to vitamin E malabsorption)
 - ↓ deep tendon reflexes, **progressive ataxia**, dysarthria, neuropathy, lower-extremity spasticity

- Ocular (related to vitamin A malabsorption)
 - Vision impairment, **retinitis pigmentosa**; strabismus, nystagmus, ophthalmoplegia (eye muscle paralysis)

DIAGNOSIS

LAB RESULTS

- ↓ ↓ triglycerides
- ↓ ↓ total cholesterol
- Lipoprotein electrophoresis → abetalipoproteinemia
- Peripheral blood-smear analysis → ↑ ↑ acanthocytes (red blood cell (RBC) with spiked membranes); normocytic anemia
- ↓ ↓ alpha-tocopherol, gamma-tocopherol (vitamin E)
- ↑ transaminases (present hepatic steatosis)

OTHER DIAGNOSTICS

- Sensory nerve conduction studies
 - Reduced nerve action potential amplitude; normal conduction velocity

TREATMENT

OTHER INTERVENTIONS

- Address neurological symptoms
 - Vitamin E
- Address gastrointestinal symptoms
 - Reduced fat-intake
- Supplement fat-soluble vitamins
 - A, D, K



Figure 43.1 Accumulation of lipids in the enterocytes of an individual with abetalipoproteinemia leads to a clear appearance.

FAMILIAL HYPERCHOLESTEROLEMIA

osms.it/familial-hypercholesterolemia

PATHOLOGY & CAUSES

- **Autosomal dominant** disorder → ↑ ↑ low density lipoprotein cholesterol (LDL-C) levels → early-onset atherosclerotic disease
 - Caused by receptor-mediated LDL-C catabolism-encoding gene mutation
 - Individuals often still experience ↑ LDL-C levels despite ↑ lipid-lowering therapy
 - **LDL receptor mutation** classes involve altered receptor synthesis/function
- LDL-mediated atherosclerotic plaque formation
 - Abnormal lipid metabolism → hyperlipidemia (LDL; especially those containing **B-100 apolipoproteins**) → subendothelial LDL retention → LDL oxidation → ↑ LDL by macrophages → foam cell formation → cytokine, growth factor release from foam cells → smooth muscle cell migration from vascular media to intima, fibrous cap formation, chronic inflammation → atherosclerotic plaque → cardiovascular, cerebrovascular, other sequelae potential

TYPES

Heterozygous FH

- LDL-C ≥ 160mg/dL (children); ≥ 190mg/dL adults (one first-degree relative diagnosed with premature coronary artery disease/ similar LDL-C levels)
- Positive genetic testing for LDL-C receptor defect

Homozygous FH

- LDL-C ≥ 400mg/dL, (one/both parents clinically diagnosed with FH)
- Positive genetic testing for LDL-C receptor defect

COMPLICATIONS

- Coronary artery calcification
- alvular cholesterol deposits → aortic stenosis
- **Accelerated atherosclerotic plaque formation** → **myocardial infarction** → sudden cardiac death
 - **Homozygous FH**: possible sudden cardiac death **before age 20**

SIGNS & SYMPTOMS

- Evidence of atherosclerotic cardiovascular disease (e.g. angina)
- Evidence of aortic stenosis, left ventricular outflow obstruction (e.g. exertional dyspnea)
- **Xanthoma** presence (usually before age 10)
 - **Tendon xanthomas**: **Achilles tendon** (commonly)
 - **Cutaneous xanthomas**: planar xanthomas on palms, soles of hands/ feet (may be painful)



Figure 43.2 Numerous tendinous xanthomata on the hand of an individual with familial hypercholesterolemia.

- **Xanthelasma**s: soft, yellow, cholesterol-filled plaques (usually appear on eyelid's medial aspect)
- **Corneal arcus**: white/grey ring around cornea



Figure 43.3 Xanthelasmata around the eyes of an individual with familial hypercholesterolemia.

DIAGNOSIS

- Positive family history
- Characteristic findings upon physical examination

LAB RESULTS

- Genetic testing
- ↑ total cholesterol, LDL-C (LDL > 90th percentile for age/sex)
- Normal/↓ HCL-C

TREATMENT

MEDICATIONS

- High-intensity statin therapy
- Cholesterol-absorption inhibitors
 - Monotherapy or in conjunction with statin therapy
- PCSK9 inhibitor/monoclonal antibodies
 - Binds to PCSK9 → inhibits hepatic LDL receptor-binding → ↑ LDL receptors available to clear LDL → ↓ LDL-C levels

HYPERLIPIDEMIA

osms.it/hyperlipidemia

PATHOLOGY & CAUSES

- ↑ serum total cholesterol, LDL-C
- Lipids enter circulation via exogenous pathway via gut/endogenous pathway (hepatic synthesis) → lipoproteins transport circulating lipids to various tissues

CAUSES

- **Primary**: genetic abnormalities (e.g. familial hypercholesterolemia), defective apoprotein B (familial)
- **Secondary**: Cushing syndrome, excessive alcohol intake, uncontrolled diabetes mellitus, chronic kidney/liver disease, certain drugs (glucocorticoids, beta blockers, thiazide diuretics, HIV

antiretroviral regimens, oral estrogen replacement)

RISK FACTORS

- Genetic predisposition
- Diet/other lifestyle factors (e.g. physical inactivity, high-fat diet)
- Pregnancy temporarily increases serum cholesterol
- Biologically-male > biologically-female individuals (premenopausal)

COMPLICATIONS

- Cardiovascular disease (e.g. angina, myocardial infarction)
- Cerebrovascular disease (e.g. stroke)

- Peripheral vascular disease
- Cholelithiasis
- Pancreatitis (triglycerides > 500mg/dL)

SIGNS & SYMPTOMS

- Cardiovascular/cerebrovascular disease evidence
- **Xanthomas**: cutaneous/found/along tendon sheaths (**tendinous xanthoma**)
- **Corneal arcus**

DIAGNOSIS

- Physical examination → presence of risk factors/cardiovascular disease symptoms
- History of cardiovascular disease-characteristic symptoms

LAB RESULTS

- *Fasting lipid profile*: ↑ total cholesterol, ↑ triglycerides, ↑ LDL, ↓ HDL

TREATMENT

- Address secondary hyperlipidemia causes

MEDICATIONS

- Statin therapy

OTHER INTERVENTIONS

- Non-statin therapy
 - E.g. fibrates, fish oil supplements containing eicosapentaenoic acid/docosahexaenoic acid concentrate; nicotinic acid (not as monotherapy)



Figure 43.4 Blood drawn from an individual with hyperlipidemia.

HYPERTRIGLYCERIDEMIA

osms.it/hypertriglyceridemia

PATHOLOGY & CAUSES

- Elevated serum triglyceride levels

CAUSES

Primary: genetic mutation (primary)

- Familial hypertriglyceridemia
- Familial combined hyperlipidemia
- Chylomicronemia
- Dysbetalipoproteinemia (APOE mutations)
- Lipoprotein lipase deficiency
- Apolipoprotein C-II deficiency (APOC2 mutations)
- Apolipoprotein A-V variants (APOA5 mutations)

Secondary: consequence of disease states

- Diabetes (especially poor glycemic control)
- Obesity
- ↑ refined carbohydrate diet
- Nephrotic syndrome
- Chronic renal failure
- Hypothyroidism
- Pregnancy (temporarily increased serum triglycerides)
 - Certain drugs (glucocorticoids, beta blockers, thiazide diuretics, HIV antiretroviral regimens, retinoids, oral estrogen replacement)

RISK FACTORS

- Influence of diet/other lifestyle factors (e.g. physical inactivity, ↑ fat diet)
- Genetic predisposition

COMPLICATIONS

- ↑ atherosclerotic plaque formation risk → cardiovascular, cerebrovascular events
- **Pancreatitis** (serum triglycerides > 1000mg/dL)

SIGNS & SYMPTOMS

- Clinical atherosclerosis manifestations
 - May not be evident until complications develop
- Xanthomas, xanthelasmas
 - Usually associated with hereditary forms
- **Lipemia retinalis**: creamy appearance within retinal blood vessels
 - May be seen with severe hypertriglyceridemia

DIAGNOSIS

- Physical examination → presence of risk factors/cardiovascular disease symptoms
- History of cardiovascular disease symptoms

LAB RESULTS

- **Fasting lipid profile**: ↑ triglycerides
 - **Normal**: <150mg/dL
 - **Mild hypertriglyceridemia**: 150–499mg/dL
 - **Moderate hypertriglyceridemia**: 500–886mg/dL
 - **↑↑/severe hypertriglyceridemia**: >886mg/dL

TREATMENT

- Address secondary causes

MEDICATIONS

- Statin therapy

OTHER INTERVENTIONS

- Non-statin therapy
 - E.g. fibrates, fish oil supplements containing eicosapentaenoic acid/docosahexaenoic acid concentrate; nicotinic acid (not as monotherapy)